

Human ES cell-derived MGE inhibitory interneuron transplantation for spinal cord injury

Grant Award Details

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Grant Type: Early Translational III

Grant Number: TR3-05606

Project Objective: The objective of this Development Candidate Feasibility Award is to assess the safety and efficacy of hESC-derived and human fetal inhibitory interneuron precursor cells (MGE cells) in a mouse model of spinal cord injury.

Investigator:

Name:	Arnold Kriegstein
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Neurological Disorders, Spinal Cord Injury

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$1,623,251

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 3

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Grant Application Details

Application Title:	Human ES cell-derived MGE inhibitory interneuron transplantation for spinal cord injury
Public Abstract:	<p>Transplantation of neuronal precursors into the central nervous system offers great promise for the treatment of neurological disorders including spinal cord injury (SCI). Among the most significant consequences of SCI are bladder spasticity and neuropathic pain, both of which likely result from a reduction in those spinal inhibitory mechanisms that are essential for normal bladder and sensory functions. Our preliminary data show that embryonic inhibitory neuron precursor cells integrate in the adult nervous system and increase inhibitory network activity. Therefore inhibitory nerve cell transplants could be a powerful way to establish new inhibitory circuits in the injured spinal cord that will reduce bladder spasticity and attenuate central neuropathic pain. We already have proof-of-principle data that murine inhibitory nerve cells integrate in the adult spinal cord and improve symptoms in an animal model of chronic spinal cord injury. We have also recently developed methods to create human inhibitory interneurons from embryonic stem cells. This proposal will capitalize on these recent developments and determine whether our human embryonic stem cell-derived inhibitory cells can be successfully transplanted into the grey matter of the injured spinal cord and reduce neurogenic bladder dysfunction and neuropathic pain, two major causes of suffering in chronic SCI patients. If successful, our studies will lay the groundwork for a potential novel therapy for chronic SCI.</p>
Statement of Benefit to California:	<p>There are an estimated 260,000 individuals in the United States who currently live with disability associated with chronic spinal cord injury (SCI). Symptoms of chronic SCI include bladder dyssynergia reflected by incontinence coincident with asynchronous contraction of internal and external sphincters, and central neuropathic pain, both of which severely impede activities of daily living, reduce quality of life, and contribute to the very high medical costs of caring for the Californians who suffer from chronic spinal cord injury. The Geron trial for SCI, as well as other cell-based approaches, aim to treat acute SCI. This proposal considers a different potentially complementary cell-transplantation strategy that is directed to more chronic SCI with the goal of improving bladder function and reducing pain. We propose to use cell grafts of inhibitory interneurons that we have derived from human stem cells in order to provide a novel treatment. If successful, we will have defined a therapeutic option that targets the most prevalent population of spinal cord injured patients. As the country's most populous state, California has the largest number of patients with chronic SCI, approximately 12,000. The estimated economic cost to California in lost productivity and medical expenses amounts to \$400,000,000 annually. The potential savings in medical care costs, and improvement in quality of life will therefore have a disproportional benefit to the state of California.</p>

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